REMARKS

Claims 2, 6, 10, 15-21, 24 and 28-29 remain finally rejected under 35 U.S.C. § 103(a) as being unpatentable over Yiv et al., U.S. Patent 6,245,349 in view of Weder WO 96/37192.

The examiner asserts that Yiv uses methods of preparing nanodispersions that do not need high shear mixing equipment, pointing to col.8, lines 19ff. The examiner admits that Yiv does not use ethanol but asserts that it is taught. The examiner asserts that WO '192 teaches similar dispersions using ethanol.

Applicants respectfully traverse this rejection for the reasons that follow.

Yiv et al., U.S. Patent 6,245,349, is entitled DRUG DELIVERY COMPOSITIONS SUITABLE FOR INTRAVENOUS INJECTION. Yiv discloses injectable drug delivery compositions comprising

- between 3 and 50 percent by weight of a phospholipid,
- between 3 and 50 percent by weight of a compound selected from the group consisting of propylene glycol and polyethylene glycol having a weight average molecular weight of from 200 to 4000, and mixtures thereof, and
- between 3 and 50 percent by weight of a high HLB surfactant having an HLB value of at least about 12.

Weder, WO 96/37192, teaches the therapeutic or cosmetic use of sphingolipids and how to enable the preparation of suitable topical or parenteral dosage forms containing this specific active ingredient.

The examiner has stated that using ethanol to form an aqueous dispersion is conventional and dependant on the utility of the formulation. However, the '192, reference does not teach that ethanol is an essential component. On page 19 different pharmaceutical formulations are disclosed which include those which are free of ethanol. Hence the use of ethanol to form an aqueous dispersion is an optional expdient.

In summary, Yiv teaches injectable drug delivery systems comprising propylene glycol and/or polyethylene glycol as essential components, and Weder teaches drug and cosmetic compositions comprising sphingolipids as an essential component, with ethanol as an optional component. There are multiple differences between the injectable drug delivery systems of Yiv and Weder's drug and

cosmetic compositions. Since a proper combination of thes references would retain all the essential components, applicants aver that only hindsight would enable one to select certain optional components from one reference and to discard ess ntial components from other as is required to reconstruct the present invention. Therefore the combination of these 2 references is improper *per se*.

Nevertheless, to hasten prosecution, applicants submit a Declaration by Dr. Andreas Supersaxo, an expert in the preparation of drug delivery systems, especially lipid based delivery systems such as liposomes, mixed micelles and microemulsions. According to said Declaration formulations 1A (propylene glycol) and 1B (ethanol) were prepared according to Example 4 of US 6,245,349 (Yiv et al.), and formulations 2A (ethanol) and 2B (propylene glycol) were prepared according to Exampl 16 of the present application. Thus formulations 1B and 2A represent the invention.

Discussing the test results on page 3, the expert commented that the data presented in Table 1 show that the Hydrocortisone formulation (Example 4, US Patent No 6,245,349) and the Vitamin A Palmitate formulation (Example 16, present application) can be prepared with both propylene glycol and ethanol. Dr. Supersaxo noted that the particle size of the ethanol based formulations was somewhat larger than the propylene glycol based ones. However, using ethanol instead of propylene glycol resulted, especially in the case of the Vitamin A Palmitate formulation, in significantly more homogenous formulations. The expert pointed out that this is an important advantage since a homogenous formulation is a prerequisite to get a reproducible drug distribution and hence drug effect.

Finally the expert declared that this behavior could not be expected by a person having ordinary skill in the art. Certainly neither Yiv et al. nor Weder teaches or suggests any advantage to replacing propylene glycol by ethanol.

Reconsideration and withdrawal of the rejection of claims 2, 6, 10, 15-21, 24 and 28-29 under 35 U.S.C. § 103(a) as being unpatentable over Yiv et al., U.S. Patent 6,245,349 in view of Weder WO 96/37192, is respectfully solicited in light of the remarks *supra* and the accompanying declaration.

Since there are no other grounds of objection or rejection, passage of this application to issue with claims 2, 6, 10, 15-21, 24 and 28-29 is earnestly solicited.

Applicants submit that the present application is in condition for allowance. In the event that minor amendments will further prosecution, Applicants request that the examiner contact the undersigned representative.

Respectfully submitted,

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Enclosures: Petition for Extension of Time, Declaration

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